Claim Rejections Under 35 U.S.C. §112, First Paragraph: Enablement

According to section five of the Office action, claims 25, 50-52 and 55-63 presently stand rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Office action on page 3 alleges that the "binding moiety broadly encompasses any sort of molecule, provided only that it binds to SEQ ID NO: 47."

During the February 5, 2003 telephonic interview, the Office indicated that the introduction of the limitations of claims 56 and 59 into independent claim 55 via a Markush group, together with the cancellation of dependent claims 56, 59 and 60 may overcome this rejection. Claims 55 and 57 have been amended, and claims 56, 59 and 60 have been cancelled. Applicants submit that the "binding moiety" language is not included in pending claims 62 and 63, and that it appears that no other basis for the rejection of claims 62 and 63 was provided in the October 23, 2001, Office action.

In view of the foregoing, Applicants believe that the claim amendments and cancellations overcome this rejection, and respectfully request that the rejection be reconsidered and withdrawn.

Objection Under 35 U.S.C. §132: New Matter

According to section six of the Office action, the paper filed July 30, 2001 is objected to for introducing new matter. The Office action suggests that Applicants' incorporation of certain teachings of Honoré *et al.* (1994) Gene 151: 291-296 (the "Honoré Publication") is improper because the incorporation-by-reference language in the specification "is drawn specifically to a protein sequence, IEF SSP 9502, and ... fails to provide support for [the incorporated] nucleic acid sequence." Applicants respectfully traverse this objection, and submit that the amendment does not introduce new matter.

The specification of the instant application clearly teaches methods for the detection of cervical cancer by detecting, for example, the presence of a cervical cancer-associated protein, for example, IEF SSP 9502, or a nucleic acid sequence encoding at least a portion of such a cervical cancer-associated protein (see, for example, page 11, lines 7-16, page 16, lines 8-12, and page 23, line 23 to page 25, line 3 of the application as filed). With regard to one cervical cancer-associated protein of interest, namely IEF SSP 9502, the specification identifies and incorporates-by-reference the disclosure of the Honoré Publication. For example, page 7, lines 14-15 of the specification includes the statement, "Honore *et al.* (1994) *Gene* 151:291-296, the *disclosure* of which is incorporated herein by reference" [emphasis added].

Also, page 47, lines 1-10 of the specification, where the Honoré Publication is discussed again, states:

> The complete amino acid sequence for this protein, as derived from a *gene* sequence, is shown in SEQ ID NO.: 10 ... The predicted molecular weight of the nuclear phosphoprotein, based upon its *nucleotide sequence* is 55 kDa, whereas its observed molecular weight by 2-D gel analysis is 79 kDa (Honoré *et al.* (1994) *supra*). [Emphasis added].

On at least several occasions, Applicants referred to nucleic acid-based assays for detecting the presence of cervical cancer in a sample of interest. The specification clearly states (for example, on page 11, lines 7-16, and on page 16, lines 8-12 of the application as filed) that the skilled artisan may detect the presence of a nucleic acid encoding a cervical cancer-associated protein (for example, IEF SSP 9502) as a way to detect cervical cancer in a sample. Also, the nucleic acid-based detection method of originally filed claim 24 includes the detection of a nucleic acid encoding a cervical cancer-associated protein having, for example, a molecular weight of about 47,900 Daltons and an isoelectric point of about 5.6. Applicants submit that Tables 2 and 4 of the specification clarify that the nucleic

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acid marker can be the nucleic acid encoding IEF SSP 9502. Furthermore, Figure 1 of the Honoré Publication not only includes the protein sequence of IEF SSP 9502 but also the nucleic acid sequence encoding and corresponding to the IEF SSP 9502 protein sequence.

Applicants submit that to limit the material incorporated-by-reference to the protein sequence of IEF SSP 9502 would be inconsistent with the entire specification of the application as originally filed. Applicants submit that the Office's view on this issue is inconsistent with the "incorporation-by-reference" doctrine. The Court of Customs and Patent Appeals in *In re Lund* stated that, "[a]s the expression itself implies, the purpose of 'incorporation by reference' is to make one document become a part of another document by referring to the former in the latter in such a manner that it is apparent that the cited document is part of the referencing document as it were fully set out therein." *In re Lund* 376 F.2d 982 (C.C.P.A. 1967).

Although the Office action indicates that the "incorporation-by-reference" statement follows a discussion of the IEF SSP 9502 protein, the language of the statement neither expressly or otherwise limits the "incorporation-by-reference" solely to the protein sequence. Given the language used in the incorporation-by-reference statement, the teachings of the specification (for example, the references to the nucleic acid-based assays discussed above), and the claims (see, the discussion of claim 24), it is apparent that the Applicants intended to incorporate-by-reference both the amino acid sequence of the IEF SSP 9502 protein and the nucleotide sequence encoding the IEF SSP 9502 protein.

In accordance with the requirements of MPEP 608.01(p), Applicants provide an executed declaration by the undersigned declaring that the nucleic acid sequence included in the amendatory material (namely, the nucleic acid sequence encoding IEF SSP 9502) is the same as that appearing in the Honoré Publication.

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In view of the foregoing, Applicants respectfully submit that the nucleic acid sequence encoding the IEF SSP 9502 protein in the Honoré Publication is properly incorporated-by-reference, and that this material does not constitute new matter. Applicants submit that the incorporation of the amendatory material is proper, and respectfully request that the objection be reconsidered and withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph: Written Description

According to section seven of the Office action, claims 24-25, 50-52 and 54-63 presently stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. The Office action states that the "claims recite SEQ ID NO: 47, which is not supported by the disclosure as filed." Applicants traverse this rejection and respectfully request that this rejection be reconsidered and withdrawn.

As discussed above, Applicants submit that the incorporation of the nucleic acid encoding the cervical cancer-associated protein IEF SSP 9502 (SEQ ID NO: 47) does not introduce new matter. In view of the foregoing comments, Applicants submit that the nucleic acid sequence of SEQ ID NO: 47 should properly be considered to constitute part of the specification as originally filed. Furthermore, Applicants submit that the record clearly demonstrates that the Applicants were in possession of the invention (i.e., the use of a nucleic acid or a peptide nucleic acid binding moiety that binds specifically to a nucleic acid encoding the cervical cancer-associated protein IEF SSP 9502 to detect cervical cancer in a sample) as of the effective filing date of the instant application.

In addition to the previous discussion about the content of the specification in relation to the new matter issue, Applicants again draw the Office's attention to claim 24 as originally filed. In particular, claim 24 relates to a method of detecting cervical cancer comprising detecting the presence of a "nucleic acid molecule" encoding a cervical cancer-associated protein including, for example, "a protein

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having a molecular weight of about 47,900 Daltons and an isolelectric point of about 5.6." Applicants submit that it is apparent from Tables 2 and 4 of the specification that at least one cervical cancer-associated protein referred to in originally filed claim 24 is IEF SSP 9502.

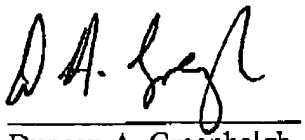
Applicants respectfully submit that in view of the teachings in the specification, for example, page 7, lines 8-15, page 11, lines 7-16, page 16, lines 11-12, the first paragraph of page 47 and claims 24 and 25 as filed, it is clear that the Applicants were in possession of the invention as claimed. In view of the foregoing, Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing amendments and comments, Applicants respectfully request that the outstanding objections and rejections be reconsidered and withdrawn. The Examiner is invited to contact the undersigned with any questions or comments about this paper. Please charge any additional fees to Deposit Account No. 20-0531.

Early favorable action is respectfully solicited.

Respectfully submitted,



Date: March 12, 2003
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MARKED-UP COPY OF THE AMENDED CLAIMS

55. (Amended) A method for detecting cervical cancer in a human, the method comprising:

(a) contacting a tissue or body fluid sample from the human with a binding moiety selected from the group consisting of a nucleic acid and a peptide nucleic acid that binds to a target nucleic acid indicative of cervical cancer, if present in the tissue or body fluid sample, to produce a complex comprising the binding moiety and the target nucleic acid, wherein the binding moiety [is capable of binding] binds specifically to a nucleic acid having a sequence set forth in SEQ ID NO: 47 or a sequence complementary thereto; and

(b) detecting the complex, which if present in the sample is indicative of cervical cancer in the human.

57. (Amended) The method of claim [56] 55, wherein the nucleic acid is from 8 to 100 nucleotides in length.

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